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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,286	09/10/2003	Yaoguang Liu	MR929-911	3489

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ROSENBERG, KLEIN & LEE
3458 ELLICOTT CENTER DRIVE-SUITE 101
ELLICOTT CITY, MD 21043

EXAMINER	
AKHAVAN, RAMIN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Applicant 06/14/04 RA

Office Action Summary	Application No.	Applicant(s)	
	10/658,286	LIU, YAOGUANG	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-9 are under consideration in instant application. A preliminary amendment to the specification, filed 03/11/2004, has been entered.

Priority

Claims 1-9 are pending and currently under examination. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Applicant seeks the benefit of priority under 35 U.S.C. 119 with regard to Chinese Application No. 02134869.3, filed 09/30/2002. However, Applicant has not perfected the claim for priority because an English translation has not been provided. Therefore, the priority date for the purposes of prior art is the filing date of instant application – 09/10/2003. To perfect the claim of priority Applicant must submit a certified English translation of the foreign priority document.

Drawings

Figure 7 is objected to because the details of the photographic reproduction are not discernable. A corrected drawing sheet is required in reply to the Office action to avoid abandonment of the application. Any amended replacement sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for

consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

On pages 14-15 and 21-23, the specification discloses sequences that are not properly identified with sequence identifiers (i.e. "SEQ ID NO:"). Sequence Listing, See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02. If said sequences were originally submitted in both electronic and paper format, then applicant is only required to make proper amendment to the Brief Description of the Drawings (i.e. with proper sequence identifiers). However, if applicant has not previously submitted said sequences then a new submission is also required (i.e. CD-ROM/CD-R, Paper Format and Attorney Declaration).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 contains an internal conflict, which confers ambiguity and indefiniteness. The preamble recites a method of producing "multi-gene recombinant vector constructs", but subpart (2) recites that either genes or DNA fragments can be inserted into the acceptor vector. Because DNA fragments may consist of non-coding regions the completed vector construct may contain a single or no gene at all. Therefore, as written the claim could be interpreted to be drawn to a vector construct that is not multi-gene and even not contain a gene altogether. As such the body of the claim does not related to the preamble, thus making the claim indefinite.

In addition, Claim 1 recites the term "DNA swapping" which does not appear to be specifically defined in the specification. It is unclear how swapping is to be interpreted with respect to acceptor and donor vectors. In addition, the claim recites the phrase "multiple donor vectors will be rotatively used", which is vague and indefinite. The particular term "rotatively" does not appear to be defined in the disclosure and is vague and indefinite. For example, as written it is unclear whether a single donor vector or multiple donor vectors are used simultaneously or sequentially with respect to the acceptor vector.

Claim 2 recites the term "RS" without first defining the corresponding meaning. For example, if applicant intends RS to stand for "Recombination Site" then it would be remedial to make the appropriate correction. Similarly, the term "S1" is vague and indefinite, as the corresponding meaning or definition has not bee provided in the claims. In addition, the claim recites the term "irreversible specific recombination" which is vague and indefinite. A more

precise term would be "irreversible site-specific recombination".

Claims 3-5 and 8 are unclear and indefinite because they recite, "donor vector I" or "donor vector II". It is understood that the references "I" and "II" refer to a first and second donor vector. However, by using the indicated references (i.e. I and II) the claims are made somewhat unclear. The base claim 1 indicates that there can be additional donor vectors, but as written the claims 3-5 and 8 confer ambiguity as to whether additional vectors are to be referenced as "I" or "II", or whether such additional vectors are wholly separate and distinguishable from "donor vector I" or "donor vector II".

Claims 3 and 4 recite the term "specific recombination" which is unclear and vague. For example it is unclear whether the term is to be interpreted as "site-specific recombination" or merely a recombination event that is somehow "specific" (e.g. homologous recombination via specific sequences). Furthermore, claim 3 recites S2 without first defining the corresponding term (e.g. "site 2").

Claim 5 recites the phrase "by alternate use of said donor vector I and donor vector II together with said acceptor vector... ". As written this claim is vague and indefinite, because while the term "alternate" confers a substitution, the conjunction "and" is used, as between vector I and vector II, indicating both vectors are to be used in concert. Therefore the claim is internally conflicting, thus unclear. Claim 5 recites the limitations "the target gene or genes", "the backbone sequence", "the second target gene or gene groups" and "the second gene or gene group". There is insufficient antecedent basis for these limitations in the claim.

Claims 6-8 are vague and indefinite because they recite that the compositions claimed (i.e. vectors) comprise "[a] part of...[claimed sequences]", which are identified through sequence

identifiers. It is unclear how the term "part of" is to be interpreted in determining the metes and bounds of the claims.

Claim 9 is vague and indefinite because it recites the term, "application" when referring to the method of claim 1. It is unclear how application is to be interpreted. Furthermore, the claim recites, "genes combined ... are transferred together ...into selected recipients...to obtain multiple gene-products or express multi-gene depended characters." As written, it is unclear what are "selected recipients" or "depended characters".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-9 are rejected under 35 U.S.C. 102(a) as being anticipated by Lin et al. (PNAS, May 13, 2003; 100(10): 5962-67; see whole document).

The broadest claim is drawn to a method of making a multi-gene recombinant vector construct where an acceptor vector and at least two donor vectors facilitate through DNA recombination assembly of a multi-gene construct. Additional embodiments include the acceptor vector comprising a recombination site (RS), an endonuclease or irreversible specific recombination site (S1), a selection marker and a replicon. Donor vectors comprise RS, S1,

selection marker different from acceptor and multiple cloning sites (MCS). Additional embodiments involve plasmid cointegration and vector-backbone removal.

Lin et al. teach a multigene assembly and transformation vector system. The system comprises an acceptor vector and two donor vectors each of which can contain a target gene or DNA fragments comprising target genes. (e.g. Abstract, p. 5963, Fig. 1; p. 5965 Fig. 2). The plasmids taught contain RS (e.g. *loxP*), S1 (e.g. I-SceI), MCS, replicon (e.g. P1 replicon). (e.g. p. 5963, Fig. 1). In addition, the reference teaches plasmid cointegration and vector backbone removal. (e.g. p. 5963, col. 2; p. 5965, Fig. 2). Furthermore, expression of multi-genes is shown through RT-PCR analysis (e.g. p. 5966, Fig. 5). In sum, Lin et al. anticipates the rejected claims.

3. Claims 1 and 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Sosio et al. (Nuc. Acids Res. May 2001; 29(7e37): 10-8; see whole document).

Claim 1 is drawn to a method of producing a vector construct comprising an acceptor vector and at least two donor vectors and a recombination system allowing two or more rounds of gene assembly by sequential DNA delivery into the acceptor vector via DNA "swapping". Claim 1 is interpreted as broadly as reasonable to comprise making a vector construct that comprises gene(s) or DNA fragments. (*See supra*, 112 ¶ 2 Rejection; explaining the internal conflict between the claim's preamble and body). In addition, the term "swapping" is interpreted to mean that through a recombination event, segments previously in a "donor vector" end up in an acceptor vector. Furthermore, the donor vectors are "rotatively used" in different rounds of recombination to allow "sequential insertion of genes or DNA fragments into the acceptor vector". "Rotatively use" is broadly interpreted to indicate that the different donor vectors are

not used simultaneously. (*See supra*, 112 ¶ 2 Rejection; noting the indefiniteness of the term "rotatively"). Dependent claims 6-8 are drawn to compositions of an acceptor or donor vectors comprising a "part of" identified sequences (i.e. SEQ ID NOs: 1-3). Interpreted broadly, the term "part of" can mean a single nucleic acid.

Sosio et al. teach a vector system comprising donor vectors and an acceptor vector for assembly of large genomic through recombination in *E. coli* cells. Target genes or inserts are exchanged between donor and acceptor vectors through recombination. (e.g. p. 3, col. 1, under Homologous Recombination). Sosio et al. teach that iterative rounds of recombination can occur between plasmids, thus necessarily there are multiple donor vectors. (e.g. p. 1, col. 2, ¶¶ 1-3). Sosio et al. teach an acceptor and donor vectors, which necessarily comprise sequences (or at least a nucleotide), that are "part of" SEQ ID NOs: 1-3.

In addition, Sosio et al. teach that the constructs can be used to mobilize gene(s) into a proper host for expression of the desired gene product(s). (e.g. p. 8, col. 1). In sum, Sosio et al. anticipate the rejected claims.

4. Claims 1, 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Connor et al. (Science, 1989; 244:1307-12; see whole document).

The claims are drawn to a method of making a vector construct, method of producing multiple gene products and compositions of acceptor vector as well as donor vectors, which through a DNA recombination system, insert multiple DNA fragments into the acceptor vector. (*See Supra*, under 102(b) Rejection, NO. 3, for further clarification of claim interpretations).

O'Connor et al. teach a acceptor vector (i.e. F Plasmid) and multiple donor vectors (i.e. shuttle plasmids) which through repeated rounds of recombination produce an F plasmid

increasing in size equivalent to inserts contained within the shuttle plasmids. (e.g. p. 1307, col. 2, ¶ 2; p. 1308, Fig. 1 and col. 1, ¶ 2 bridging to col. 2, ¶ 1). The final co-integrated F plasmid can comprise more than one gene (i.e. Ubx and abdA genes). (e.g. p. 1308, col. 2, ¶ 2). Furthermore, an intrinsic property of cloning large DNA fragments (e.g. 136 kb) is that an entire small chromosome (i.e. multiple genes) can be comprised therein. (e.g. p. 1312, col. 1, ¶ 1). The plasmid taught contains at least a single nucleotide of SEQ ID NOs: 1-3. In addition, O'Connor teaches that the vector system is used to examine gene products through reintroduction into an appropriate host organism. (e.g. p. 1312, col. 1, ¶ 4). In sum, O'Connor et al. anticipate the rejected claims.

5. Claims 1, 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Hartley et al. (US 6,270,969 B1; see whole document; hereinafter '969 patent).

The claims are drawn to a method of producing a recombinant vector, method of producing multiple gene products, as well as compositions of donor and acceptor vectors comprising parts of SEQ ID NOs: 1-3. (*See Supra*, under 102(b) Rejection NO. 3 for further clarification of claim interpretations).

The '969 patent teaches a method of recombinational cloning between acceptor and donor vectors that produce a vector construct comprising multiple DNA segments. (e.g. Abstract). More particularly, the '969 patent teaches that the donor and acceptor vectors undergo specific recombination to produce co-integrated vector constructs. (e.g. col. 19, Example 1). The '969 patent teaches more than one donor vector. (Id.). Furthermore, the acceptor or donor vectors comprise at least part of SEQ ID NOs: 1-3 (i.e. at least a single nucleotide). In addition the constructs/system are able to produce gene products (e.g. col. 20, ll. 25-38; showing that

several antibiotic resistance gene products are produced). In sum, the '969 patent anticipates the rejected claims.

6. Claims 1 and 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Cheo et al. (US 2002/0007051 A1; see whole document; hereinafter Cheo)

The claims are drawn to a method of recombinational cloning to produce a vector construct, method of producing gene products and compositions of donor as well as acceptor vectors. (*See Supra*, under 102(b) Rejection NO. 3 for further clarification of claim interpretations).

Cheo teaches multiple donor vectors each containing a DNA insert, which is mobilized into an acceptor vector through a recombination system. (e.g. Figs. 2-9). More particularly Cheo teaches that recombination between two different starting vectors occurs with a "Destination vector" (i.e. acceptor vector). (e.g. p. 54, ¶ 0482, Example 1). The document is replete with examples of multiple constructs recombining with an acceptor vector to produce constructs that comprise multiple DNA segments. (e.g. Figs. 2-9; p. 57, Example 2; p. 60, Example 5; p. 64, Example 7). Furthermore, Cheo teaches transfer of the acceptor vector constructs into cells for gene product expression. (e.g. p. 77, Example 17; p. 78, Example 18; showing multiple genes, i.e. luxA-E). Vectors taught necessarily contain parts of SEQ ID NOs: 1-3. Therefore, Cheo anticipates the rejected claims.

7. Claims 1 and 6-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Borokov et al. (WO 01/11058 A1; see whole document; hereinafter Borokov).

The claims are drawn to a method of recombinational cloning to produce a vector construct, method of producing gene products and compositions of donor as well as acceptor vectors. (*See Supra*, under 102(b) Rejection NO. 3 for further clarification of claim interpretations).

Borokov teaches vectors and cloning methods where multiple donor and acceptor vectors recombine to form a vector construct comprising multiple DNA segments. (e.g. Abstract; Fig. 4). More particularly, Borokov teaches a "Gene Stacking Approach" where new genes are sequentially added to an existing vector construct through a recombination system. (e.g. p. 28, Example 5). Furthermore, gene products are expressed in an appropriate host (e.g. potato). (e.g. p. 32, Example 6). In addition, the vectors taught necessarily contain at least a part of the SEQ ID NOs 1-3, in instant application. Therefore, Borokov anticipates the rejected claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ramin (Ray) Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached on Monday- Friday from 8:00-4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GERRY LEFFERS
PRIMARY EXAMINER